NO and CO Transfer

In a recent issue Moinard and Guenard [1] have measured membrane diffusing capacity (DM) and pulmonary capillary blood volume (Qc) by simultaneous NO and CO transfer. Their method [2] assumes that the specific conductance of blood for NO (\(\Theta_{NO}\)) is effectively infinite and therefore that DLs\(\text{NO}\) approximates DMs\(\text{NO}\). Unfortunately these assumptions are now known to be incorrect casting doubt on their measurements of DM and Qc.

Firstly, we have recently found that DLs\(\text{NO}\) depends to a similar extent to DLs\(\text{CO}\) on haemoglobin concentration [3]. According to Roughton and Forster's model [4] DM should be independent of haemoglobin concentration. Our finding therefore suggests that \(\Theta_{NO}\) makes a significant contribution to DLs\(\text{NO}\). Secondly \(\Theta_{NO}\) may be calculated in an analogous way to \(\Theta_{CO}\) [4] from continuous flow measurement of the rate of reaction of NO and red cells [5]. In traditional units:

\[
\Theta_{NO} = 0.0166 \text{mM l \text{CO} \text{Pa}^{-1}}
\]

where \(j^c\) is the average value for the rate constant for nitric oxide uptake by human red cells =167 mM l sec\(^{-1}\) [5], 0.2 is the capacity of blood for binding NO in ml gas STPD ml of blood \(^1\) and 60 is seconds minute\(^{-1}\). \(\Theta_{NO}\) is plasma (water) solubility of NO at 37\(^\circ\)C [6] = 0.041 ml ml\(^{-1}\) atm\(^{-1}\)=0.0022 mM torr\(^{-1}\)=0.0166mM kPa\(^{-1}\).

In SI units \(\Theta_{NO} = j^c \times 0.0166 \times 0.60 = 1.5 \times 10^3 \text{ mM per min} \times \text{ kPa} \times \text{ L} \times \text{ ml} \times \text{ dm} \text{-}1\) in mmol L\(^{-1}\).

These measurements of \(j^c\) were made in the absence of oxygen and at 38\(^\circ\)C. However variation of temperature and oxygen concentration alter \(\Theta\) via the chemical reaction with haemoglobin [4]. Since the rate of reaction of NO with haemoglobin is extremely rapid \(j^c\) is believed to be a measure of diffusive conductance of the red cell only [5]. Accordingly this value for \(j^c\) can be used to calculate \(\Theta_{NO}\) for normoxia and normal body temperature. DMs\(\text{NO}\), DMs\(\text{CO}\) and Qc may then be correctly calculated by solving

\[
\frac{1}{DL} = \frac{1}{DM+1/\Theta_{Qc}}
\]

for each gas by inserting appropriated values for \(\Theta_{CO}\) and \(\Theta_{NO}\) and assuming DMs\(\text{NO}/DMs\text{CO}=\text{the ratio of Krogh diffusion coefficients NO/CO}=2 [2]). The ratio of DLs\(\text{NO}\) divided by DLs\(\text{CO}\) of about 4, that has been observed by ourselves [7] and others [8] is therefore explained: it lies between DMs\(\text{NO}/DMs\text{CO}(=2)\) and \(\Theta_{NO}/\Theta_{CO}(=5-7\) depending on the estimate of \(\Theta_{CO}\) used).

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References
2. Guenard H, Varne N, Vada P. - Determination of Lung capillary blood volume and membrane diffusing capacity in man by the measurement of NO and CO transfer. Respir Physiol, 1987, 70, 113-120.

There is, at least, one good agreement among works in the field of NO and CO transfer, including your work; the ratio TLs\(\text{NO}\) and DMs\(\text{CO}\) is about 5.

If the relationship between TLs\(\text{NO}\) and DMs\(\text{CO} \cdot \text{Qc}\) is:

\[
1/\text{TLsNO} = 1/(a \times \text{DMsCO}) + 1/(k \times \Theta_{CO} \times \text{Qc})
\]

where \(a = (\sqrt{\text{MCO}/\sqrt{\text{MNO}}}) \times (\Theta_{NO}/\Theta_{CO})\), \text{M}\(\text{CO}\) and \text{M}\(\text{NO}\) being the molecular weight and the solubility respectively, and \(k\) is \(\Theta_{NO}/\Theta_{CO}\), where \(\Theta\) is the specific conductance of blood. Taking into account your value of \(\Theta_{NO}(4.4 \text{ mm} \text{ min}^{-1} \text{ torr}^{-1})\) and \text{CO} value from Forster for a \(\text{Po}_2 = 100 \text{ torr}\) [1] (0.58 \text{ mm} \text{ min}^{-1} \text{ torr}^{-1}), \(k=7.58\).

The above equation can be written [2]:

\[
1/\text{DLsNO} = 1/(\text{DMsCO}) + 1/(k \times \Theta_{CO} \times \text{Qc})
\]
\[
(1 - \frac{a}{k}) / \text{DMco} = \frac{a \times \text{TLno} - (a/k)}{\text{TLco}}
\]
with \( \text{DMco} = b \times \text{TLco} \)
\[
\text{TLno/TLco} = a / [1 - (a/k) / b + (a/k)]
\]

With \( a = 1.97 \), \( a/k = 0.26 \), \( \text{TLno/TLco} = 5 \), the "b" calculated value is then 5.7, \( i.e. \) the DMco value should be about six times greater than TLco, result which seems rather uncommon. Making the assumption that \( k \) is far greater than "a", \( a/k \) ratio becomes negligible compared to unity and the calculated "b" value is then 2.5 which seems to be in close agreement with the usual reported values.

Our personal knowledge of the effect of anaemia on TLno transfer is scarce. Ten anaemic patients, haemodialysed for chronic renal failure, performed TLno/TLco transfer manoeuvres at least two days after haemodialysis. Using our calculation procedure a decrease in DMco was found, as Qc remained normal. Using your \( \text{Ohno value, DMco would increase and Qc would decrease. This situation seems rather unexpected in patients with an increase of 2 to 3 litres in water body content in two days. No correlations were found between Hb concentration and either TLno or TLco, suggesting that other factors are determinant in these transfers.}

The chemistry of NO in total blood seems rather complex to our non specialist point of view. We tried to summarize this complexity in our first article [2]. As you mentioned, f’c "is believed to be" a measure of diffusive conductance of the red cell only. The fact that f’c value was derived from free-oxygen red cell suspensions is likely to be determinant. Until the chemistry of NO in the \textit{in vivo} conditions is better known, it seems wise to restrict our discussion to more global and accurate findings, such as NO and CO transfer.

Finally I would point out, without any polemic perspective, that referring to an abstract is not nowadays a fair scientific procedure. Abstracts are too many, and articles are a lot. When I learned physiology my main mentor told me: "that it was better to publish, new and uncertain or sulfurous ideas in abstract form in a "nobody know, but I" journal, like the "Low Ohio River journal of medicine" (I guess this journal doesn't exist). If the subject remained in the shadow nobody would care about it, but if someone finds results in agreement with yours you could thus claim your anteriority". We laughed on that twenty years ago and then speculated on the feasibility of DM and Qc measurements using the transfer of two gases. At that time we thought about CO and \( \text{SH}_2 \). Thanks to late Pr. BARGETON.

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References

2. Guenard H, Varene N, Vaida P. - Determination of lung capillary blood volume and membrane diffusing capacity in man by the measurement of NO and CO transfer. \textit{Respir Physiol}, 1987, 70, 113-120.